REMARKS

Reconsideration of the restriction requirement and the election of species is respectfully required.

Claims 1-50 are pending in the application. Claims 1-20 and 42-50 were provisionally elected, with traverse, by Applicants' undersigned attorney. Claim 51 has been added in response to the election of species requirement. Accordingly, claims 1-51 are presently under examination.

Minor changes in the specification, including the correction of two literature citations, have been made for the sake of accuracy and completeness. No new matter has been entered by any of the foregoing amendments to the specification.

In order to comply with the Examiner's request with respect to the election of species requirement, claim 51 has been added above. Claim 51 recites "a modified nucleotide compound which comprises at least one component selected from the group consisting of MN_3M, BN_XM and $M(N)_XB$. In the species defined by claim 51, N comprises a phosphodiester-linked modified 2'-deoxynucleoside moiety; M is a moiety that confers endonuclease resistance on said component and which comprises at least one nucleic acid base modified with a 3'-methylphosphonate; B is a moiety that confers exonuclease resistance to the terminus to which it is attached and comprises a 2',3'-dideoxyribose nucleotide; and x is an integer of about 2.

The Restriction Requirement Under 35 U.S.C. §121

In the Office Action (page 2), the Examiner required restriction to one of the following groups:

I. Claims 1-20 and 42-50, drawn to nuclease resistant oligonucleotides, classified in Class 536, subclass 27;

II. Claims 21-39, drawn to a method of inhibiting the function of an RNA, classified in Class 435, subclass 6; and

III. Claim 40, drawn to a method of identifying a specific compound having nuclease resistance and the ability to form an RNase H substrate when in complex with an RNA.

Applicants hereby affirm the election of Group I, claims 1-20 and 42-50. Applicants respectfully request that the restriction requirement under 35 U.S.C. §121 be reconsidered and withdrawn in view of the remarks set forth below.

Applicants respectfully submit that the claims represented by Groups I, II and III, as set forth hereinabove, form a single general inventive concept which should properly be examined in the same application. Applicants contend that a diligent search of the art of any one of Groups I, II or III, as classified by the Examiner, would necessitate a review of the art of the other corresponding groups.

Under MPEP §803, two criteria are necessary in order for a restriction requirement between patentably distinct inventions to be proper:

(1) The inventions must be independent or distinct as claimed; and

(2) there must be a serious burden on the Examiner if restriction is not required.

It is respectfully submitted that a search of the prior art to include the method of inhibiting the function of an RNA (defined by claims 21-39) and the method of identifying a compound having nuclease resistance/ability to form an RNAse H substrate (defined by claim 40), would not place a serious burden on the Patent Office or the Examiner in light of the search that will already be required for the elected claims 1-20 and 42-50. All of claims 1-50 ultimately recite the modified nucleotide compounds disclosed in the specification, or their use in methods of identification or treatment. Furthermore, even assuming for the sake of argument, that the subject matter of claims 21-42, would entail, for example, a separate classification or status in the art from the subject matter of claims 1-20 and 42-50, Applicants are firmly of the opinion that such a search, diligently undertaken, of the subject matter covered by Groups II and III, would inevitably overlap with the subject matter covered by Group I. Because the Examiner is expected to carry out a diligent search of the prior art, Applicants submit that no serious burden would be imposed in terms of the search effort if he properly includes the subject matter of Groups II and III together with the subject matter of Group I - because all three groups define subject matter pertaining to modified nucleotide compounds per se or their use in methods of identification or treatment.

Applicants sincerely believe that if the Examiner carefully considers the foregoing arguments, he too, will reasonably conclude that no burden in terms of search efforts will be placed upon the Patent Office or himself, if the claims of Groups II and III are examined in this application, together with the claims of Group I.

Applicants earnestly urge, therefore, that the Examiner withdraw the restriction requirement on the basis of the foregoing remarks.

The Election of Species Requirement Under 35 U.S.C. §121

In the Office Action (pages 3-4), the Examiner stated that "claims 1-20 and 42-50 are generic to a plurality of disclosed patentably distinct species comprising modified oligonucleotides resistant to endo- and exonucleases. The applicant is required under 35 U.S.C. §121 to elect a single disclosed species, even though this requirement is traversed."

The Examiner further stated:

> "By election of species, the Examiner means an ultimate species from which a reasonable genus will be carved. This ultimate oligonucleotide as defined by claim 1 would be one in which N, M, B and x are given specific definitions. In other words, N is to be selected as either a phosphodiester bond or a specific modified phosphate bond such as 3'-methylphosphonate. M should be defined as a specific modified base or specific unmodified base, such as adenine, etc. B should be defined as a specific compound, whether a specific protein or specific intercalating group, etc. X should be defined as a specific integer." [emphasis in original].

Applicants respectfully traverse the election of species requirement. In addition, Applicants are presenting new claim 51 which is directed to species of N, M, B and x in the disclosed modified nucleotide compound. Applicants respectfully request that the election requirement be reconsidered and withdrawn in view of the following remarks.

Applicants note that the instant invention is directed to modified oligonucleotides or polynucleotides having a sequence of two or more phosphodiester-linked nucleosides and which are nuclease resistant. Such modified nuclease-resistant nucleotide compounds include at least one component selected from the group consisting of MN_3M, $B(N)_xM$ and $M(N)_xB$ wherein N is a phosphodiester-linked modified or unmodified 2'-deoxynucleoside moiety; M is a moiety that confers endonuclease resistance on said component and that contains at least one modified or unmodified nucleic acid base; B is a moiety that confers exonuclease resistance to the terminus to which it is attached and x is an integer of least 2.

Applicants submit that the claimed modified oligonucleotides or polynucleotides compounds are novel, useful and unobvious. The originally claimed compounds and methods, which are patentably distinct from the prior art, comprise or employ those oligonucleotides or polynucleotides which, as a generic group, have a combination of nuclease resistance and the ability to form an RNase substrate when in complex with an RNA. It is respectfully submitted that the species of oligonucleotides and polynucleotides disclosed and claimed in the instant application form a single general inventive concept, and moreover, they represent a reasonable number of species for the members of N, M, B and x which have characteristics in common, such that the generic subject matter for these members - and not single individual species - should properly be examined in the same application. In addition, Applicants contend that if the species recited in new claim 51 is allowed, then the other species will also be found allowable as part of a generic claim, e.g., claim 1, in the instant invention. Applicants further contend that they are entitled to claim their invention as broadly as the prior art permits, commensurate with the disclosure requirements of 35 U.S.C. §112. Under such a well-

established legal principle, Applicants are entitled to claim and to pursue the full breadth of their generically disclosed invention in the same application. Applicants request, therefore, that the Examiner reconsider and withdraw the species election, and examine the instant claims as originally filed.

Submission of Information Disclosure Statement

In order to comply with their duty of disclosure under 37 C.F.R. §1.56, Applicants are filing, concurrently with this response, an Information Disclosure Statement under 37 C.F.R. §1.99. In the Information Disclosure Statement, Applicants are providing a copy of each of the following nineteen references:

1. van der Krol, et al., BioTechniques, 6:958-976 (1988) [Exhibit 1];
2. Inoue, et al., Nucleic Acids Syposium Series, 18:221-224 (1987) [Exhibit 2];
3. Marcus-Sekura, et al., Nucleic Acids Research, 15:5749-5763 (1987) [Exhibit 3];
4. Agrawal, et al., Proc. Natl. Acad. Sci. (USA), 85:7079-7083 (1988) [Exhibit 4];
5. Stein, et al., Nucleic Acids Research, 16:3209-3221 (1988) [Exhibit 5];
6. Sun, et al., Biochemistry, 27:6039-6045 (1988) [Exhibit 6];
7. Sarin, et al., Proc. Natl. Acad. Sci. (USA), 85:7448-7451 (1988) [Exhibit 7];
8. Quartin, et al., Biochemistry, 28:1040-1047 (1989) [Exhibit 8];
9. Maniatis, et al., Molecular Cloning: A Laboratory Manual, Cold Spring Harbor Laboratory, pp. 109-110 (1982) [Exhibit 9];
10. Minshull, et al. Nucleic Acids Research, 14:6433-6451 (1986) [Exhibit 10];
11. Cazenave, et al., Nucleic Acids Research, 15:4717-4736 (1987) [Exhibit 11];

12. Miller, et al., Biochimie, 67:769-776 (1985) [Exhibit 12];
13. Maher, et al., Nucleic Acids Research, 16:3341-3358 (1988) [Exhibit 13];
14. Smith, et al., Proc. Natl. Acad. Sci. (USA) 83:2787-2791 (1986) [Exhibit 14];
15. Agris, et al., Biochemistry, 25:6268-6275 (1986) [Exhibit 15];
16. Melton, et al., Nucleic Acids Research, 12:7035-7056 (1984) [Exhibit 16];
17. Agrawal, et al., Tetrahedron Letters, 28:3539-3542 (1987) [Exhibit 17];
18. Dash, et al., Proc. Natl. Acad. Sci. (USA) 84:7896-7900 (1987) [Exhibit 18]; and
19. Quartin, et al., Nucleic Acids Research 18:7253-7262 (1989) [Exhibit 19].

The first eighteen references were cited in the instant specification; the nineteenth reference is a paper co-authored by the instant inventors, which was published less than a year prior to the filing date of the instant application and which served in part as a basis for the application. A completed Form PTO-1449 (Exhibit 20) has also been included with the Information Disclosure Statement.

In view of the foregoing remarks, Applicants respectfully request reconsideration and withdrawal of both the restriction requirement and the election of species. Full examination of claims 1-51 on the merits is believed to be in order.

SUMMARY AND CONCLUSION

Claims 1-51 are presented for further prosecution, the restriction requirement notwithstanding. Claim 51 has been added in response to the election of species requirement. No claims have been amended or cancelled by this Response.

This Response is accompanied by and includes a Request For a One-Month Extension of Time. The Patent and Trademark Office is hereby authorized to charge Deposit Account No. 05-1135 for the requisite fee of $100.00 as set forth in 37 C.F.R. §1.17(c). In addition, an Information Disclosure Statement Under 37 C.F.R. §§1.56 and 1.99 (including Exhibits 1-20) is being concurrently filed with this Response. The Patent and Trademark Office is further authorized to charge Deposit Account 05-1135 for any other fees in connection with this Response and to credit any overpayment therein.

In view of the above discussion of the issues, Applicants respectfully submit that substantive examination of all the instant claims, 1-51, is in order. The Examiner is respectfully requested to telephone the undersigned attorney at (212) 924-5409 or 924-9578 to discuss the subject application.

Respectfully submitted,

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